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|--|-------------|-----------------------|---------------------------|------------------|
| APPLICATION NO.  | FILING DATE | FIRST NAMED INVENTOR  | ATTORNEY DOCKET NO.       | CONFIRMATION NO. |
| 10/790,746   | 03/03/2004  | Franz Paul Armbruster | 0756-0124P                | 2900             |
| 2292 7590 04/10/2007<br>BIRCH STEWART KOLASCH & BIRCH<br>PO BOX 747<br>FALLS CHURCH, VA 22040-0747 |             |                       | EXAMINER<br>HAQ, SHAFIQUH |                  |
|  |             |                       | ART UNIT                  | PAPER NUMBER     |
|  |             |                       | 1641                      |                  |
| SHORTENED STATUTORY PERIOD OF RESPONSE   |             | NOTIFICATION DATE     |                           | DELIVERY MODE    |
| 3 MONTHS   |             | 04/10/2007            |                           | ELECTRONIC       |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Notice of this Office communication was sent electronically on the above-indicated "Notification Date" and has a shortened statutory period for reply of 3 MONTHS from 04/10/2007.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

**Office Action Summary**

Application No.

10/790,746

Applicant(s)

ARMBRUSTER ET AL.

Examiner

Shafiqul Haq

Art Unit

1641

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 28 September 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-10 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-10 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |   |   |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)  | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date <u>3/3/04</u> . | 6) <input type="checkbox"/> Other: _____  |

## DETAILED ACTION

### *Status of claims*

1. Claims 1-10 are pending.

### ***Claim Rejections - 35 USC § 112***

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 1-10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.
4. Claims 1 and 4 recite the phrase "A represents a functional group, coupled via a spacer group, which can be bound by a protein with high affinity". The term "can be" is not a positive recitation and thus it can be interpreted that intended "high affinity binding of a protein" to the functional group "A" is not a required part of the invention.
5. Claims 1 and 4 recite the phrase "R represents a 25-hydroxy side-group of vitamin D<sub>2</sub> or of vitamin D<sub>3</sub>". The phrase is confusing because vitamin D<sub>2</sub> or vitamin D<sub>3</sub> do not have hydroxyl group at position 25. It is 25-hydroxy vitamin D<sub>2</sub> or 25-hydroxy vitamin D<sub>3</sub> that contains a hydroxyl group at position 25. It is unclear whether the term "25-hydroxy side-group" encompasses only the "hydroxyl group" at position 25 of the 25-hydroxy vitamin D<sub>2</sub> or 25-hydroxy vitamin D<sub>3</sub> or the term "25-hydroxy side-group" is intended to include the whole side chain that is substituted at position 17 of 25-hydroxy vitamin D<sub>2</sub> or of 25-hydroxy vitamin D<sub>3</sub>. Applicants are advised to

Art Unit: 1641

clearly define the structure of R in order to avoid further confusion. Furthermore, the chemical nature and structure of the "spacer" is not clear.

6. The method of claim 1 is vague and indefinite as to how the amount of 25-hydroxy or 1 $\alpha$ , 25-hydroxy vitamin D metabolite in the sample is measured because the method is unclear how the binding of vitamin D derivative of the formula of claim 1 to Vitamin D binding protein is correlated with the measurement of the amount of 25-hydroxy or 1 $\alpha$ , 25-dihydroxy vitamin D metabolite in the sample.
7. Claim 1 recites the phrase "method of measuring the amount of a 25-hydroxy- or 1 $\alpha$ , 25-dihydroxy vitamin D metabolite in the sample". It is unclear whether the claimed method be utilized for detection of one or 25-hydroxy- or 1 $\alpha$ , 25-dihydroxy vitamin D metabolite? Is it useful only in detection of said vitamin D derivatives when both are present in the sample?
8. Claims 1-3 and 10 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: positive steps involved in the method/process that clearly relate each step to the binding of vitamin D binding proteins to the measurement of 25-hydroxy or 1 $\alpha$ , 25-dihydroxy vitamin D metabolite in the sample. An appropriate sequence of method steps would include a step in which vitamin D derivative of the formula of claim 1 is contacted/mixed/added to the sample, a step for binding/or displacement and the detection of this binding by the use of an appropriate method steps and a step for the correlation of the

Art Unit: 1641

detection of binding with the presence/amount of 25-hydroxy or 1 $\alpha$ , 25-hydroxy vitamin D metabolite in the sample.

9. Claim 4 recites the phrase “a kit for detection of 25-hydroxy- or 1 $\alpha$ , 25-dihydroxy vitamin D metabolites comprising a standardized quantity of solid or a standardized solution of a vitamin D derivative” in lines 1-4. It is unclear what is meant by “solid” or what compounds or substances are intended to encompass by the term “solid”. It is also unclear what propose would serve by the kit wherein the kit comprises only of “solid”. It is also unclear what function the “solid” plays in the detection of 25-hydroxy- or 1 $\alpha$ , 25-dihydroxy vitamin D metabolites that is included in the kit.

***Claim Rejections - 35 USC § 102***

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. Claims 1-8 and 10 are rejected under 35 U.S.C. 102(b) as being anticipated by Holick et al. (WO 97/24127).

Holick teaches methods to assay for the presence of vitamin D analogs and their metabolites in a sample using labeled vitamin D compounds (i.e. vitamin D derivative) in the assay method (see field of invention). The vitamin D metabolites includes , 1,25 dihydroxy vitamin D<sub>3</sub>, 25 hydroxy vitamin D<sub>2</sub> etc. (page 1, lines 12-25 and page 5, lines 10-14) The labeled vitamin D derivative of Holick (see compounds

B and C of example 2 and 3 of pages 14-15) reads on the compound of the formula of claim 1 when R represents R a 25-hydroxy side-group of vitamin D<sub>2</sub> or of vitamin D<sub>3</sub>, Y=H, A= functional group coupled via a spacer group, which can be bound by a protein with high affinity (see definition of A in lines 9-16 of specification wherein A can be biotin). Holick discloses a method in which labeled vitamin D derivative is first allowed to bind to a protein capable of binding to the vitamin D derivative and which is attached to a solid support. Sample containing vitamin D metabolite is then added to effect displacement of the labeled compound from said protein and Holick discloses that preferred protein is vitamin D binding protein (DBP) (see pages 11-12). Holick discloses different immunoassay methods (page 10, lines 21-25 and page 12, lines 9-11) and solid phase support including dextran, agarose, polystyrene and microtitration plate (page 11, lines 27-29) and the solid phase can be beads, plates or tubes (page 10, lines 15-16). With regard to Kit of claim 4, Holick discloses that the labeled compounds are ideally suited for the preparation of a kit and the kit may contain labeled vitamin D derivative, vitamin D binding protein and avidin coated beads, plates etc. (page 10, lines 9-20). With regard to length of biotin group and spacing group, the length of spacers and the length of biotin and spacer of at least one of the compounds A-C and D of the reference encompass the length of 0.9 to 1.5 nm of instant application.

The recitation of the method in claims 1 and 4 to obtain the vitamin D derivative (product by process) has not given any patentable weight because the method for measuring of vitamin D metabolite with the vitamin D derivative does not depend on

Art Unit: 1641

the method of preparation of the vitamin D derivative and thus is not a limitation *per se*. Therefore, the reference is deemed to anticipate the cited claims.

***Claim Rejections - 35 USC § 103***

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

13. Claim 9 is rejected under 35 U.S.C. 103(a) as being unpatentable over Holick et al. (WO 97/24127) as described above and further in view of DeLuca et al. (US 5,064,770).

See above teaching for Holick et al.

Holick et al disclose kit comprising solid phase (e.g. beads) and vitamin D derivative but differ from the instant application in failing to disclose magnetic microparticle as solid phase.

DeLuca et al. in a binding assay to determine 1, 25-dihydroxy vitamin D receptor disclose using magnetic particle for anchoring binding molecules to the particle.

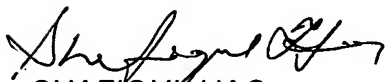
Since the use of magnetic particle is very common in the field of immunoassay and magnetic particle has been disclosed for detection of vitamin D binding protein (DeLuca et al.), it would be obvious to one of ordinary skill in the art at the time the invention is made to include magnetic particle in the method of Holick et al. for detection of vitamin D metabolites involving vitamin D binding protein with a reasonable expectation of success.


**Conclusion**

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shafiqul Haq whose telephone number is 571-272-6103. The examiner can normally be reached on 7:30AM-4:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V. Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

  
SHAFIQULE HAQ  
EXAMINER  
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LONG V. LE 03/30/07  
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